A Study of Distal Sensory Nerves in Patients with Newly Diagnosed Asymptomatic Type 2 DM

Eurasian Clinical and Analytical Medicine Original Research

A Study of Diabetic Polyneuropathy

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Abstract

Aim: This study aimed to determine the importance of Medial Plantar (MP), Dorsal Sural (DS) and Medial Dorsal Cutaneous (MDC) sensory nerve conduction studies in addition to the other routine electrophysiological studies performed in newly diagnosed Type II Diabetes Mellitus (DM) for diagnosing diabetic polyneuropathy (PNP) at an early stage.

Material and Methods: This study included a total of 35 patients aged less than 60 years with newly diagnosed, untreated Type II Diabetes, and 30 healthy volunteers who applied to the Outpatient Clinic of Internal Medicine and Endocrinology at Şanlıurfa Training and Research Hospital and Harran University Faculty of Medicine Research and Application Hospital between April 2014 and August 2014.

Results: Our study enrolled a total of 35 Type II Diabetes patients (20 females, 15 males) with a mean age of 47.22±8.15 years, and 30 healthy controls (17 females and 13 males) with a mean age of 49.30±6.56 years. The two groups did not significantly differ with respect to age and sex ($p>0.05$). MP, MDC, and DS sensory nerve conduction studies, performed additionally to the standard PNP protocol, revealed that the amplitudes and conduction velocities of each of the three nerves were significantly lower than those of the control group ($p<0.01$).

Discussion: It is possible to diagnose diabetic PNP at an early, asymptomatic stage by studying sensory nerves conduction properties of MP, MDC, and DS in addition to the standard electrophysiological PNP protocol. Detection of PNP by these methods at an early stage may help taking measures to prevent progression into symptomatic PNP.

Keywords

Diabetic Polyneuropathy; Medial Plantar Nerve; Medial Dorsal Cutaneous Nerve; Dorsal Sural Nerve

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Introduction

Signs and symptoms related to peripheral nervous system with no other apparent cause in a diabetic patient are collectively referred to as diabetic neuropathy. Diabetic neuropathy can cause a wide spectrum of abnormalities ranging from autonomic and cardiovascular abnormalities to diabetic foot ulcers. The most common type of diabetic polyneuropathy (PNP) is the distal symmetric PNP and the associated neuropathic pain [1]. It is well known that long-standing hyperglycemia causes neuropathy in diabetic patients. Neuropathy may also become manifest in the early stage of the glucose regulation disorder [2].

The neuropathy prevalence has been reported 10% in newly diagnosed Type II Diabetes patients, stressing the importance of early diagnosis of that disorder [3]. The present study aimed to determine the importance of Medial Plantar (MP), Dorsal Sural (DS) and Medial Dorsal Cutaneous (MDC) sensory nerve conduction studies (NCS) in addition to the other routine electrophysiological studies in newly diagnosed Type II Diabetes Mellitus (DM) for diagnosing diabetic PNP at an early stage.

Material and Methods

This study enrolled 35 patients aged less than 60 years with newly diagnosed, untreated Type II Diabetes, and 30 healthy volunteers who applied to the Outpatient Clinic of Internal Medicine and Endocrinology at Şanlıurfa Training and Research Hospital and Harran University Faculty of Medicine Research and Application Hospital between April 2014 and August 2014. The patients with lomber radiculopathy, mononeuropathy, and plexopathy diagnosed by neurological examination and electrophysiological studies were excluded from the study protocol. In addition, patients who had renal failure, another disease likely to cause peripheral neuropathy, drug use likely to cause peripheral neuropathy, or toxic substance exposure were also excluded from the study protocol. This study was performed in compliance with the Human Rights Declaration of Helsinki and all subjects gave informed consent before study entry. This study was approved (Approval No:74059997.050.01.04/64) by the local ethics committee of Harran University.

All patients and control subjects underwent MP, DS, and MDC sensory NCS at the ENMG laboratory, in addition to the routine PNP study protocol including the motor NCS of bilateral posterior tibial, peroneal, median, and ulnar nerves and the sensory NCS of bilateral sural, median, and ulnar nerves.

The electrophysiological studies were performed using the Nihon Kohden EMG-EP V-08 device. The skin temperatures of the subjects were kept at 31-33 °C. The conduction studies were carried out using the Ag/AgCl disk surface electrodes. Then, the subjects underwent conventional sensory and motor conduction studies of lower and upper extremities. In the nerve conduction study, the motor latency was measured with reference to the starting point of the negative deflection and the motor amplitude with reference to the peaks of the negative and positive deflections. The motor nerve examination was performed with a filter frequency of 10 Hz-5 kHz, a sweep rate of 5 msec/div, a stimulus duration of 0.2 msec, and a stimulus frequency of 1 /sec. The corresponding settings of the sensory nerve examination were 20 Hz-2 kHz, 1 msec/div, 0.2 msec, and 1 /sec, respectively.

Sensory nerve conduction studies

a) Both MP nerves were stimulated using a felt electrode in the direction of the recording electrode at a point distal to it at the medial part of the sole between the metatarsal bones and orthodromic recordings were performed from the inner malleolus over the flexor retinaculum. The nerve's conduction velocity, distal latency, and amplitude were measured.

b) Both MDC nerves were stimulated using a felt electrode in the direction of the recording electrode at a point distal to it at the medial part of the dorsum of the foot between the first and second metatarsal bones. The orthodromic recordings were performed over the 1/3 medial area on the line connecting the medial and lateral malleoli. Additionally, this nerve distal latency and sensory action potential were

Table 1. Comparison of nerve conduction data belonging to patient and control groups.

Nerve	Controls (n: 30)	Patient (n: 35)	P value
Medial plantar			
Amplitude (μV)	8.23 ± 1.99	3.95 ± 0.81	0.000*
NCV (m/sn)	55.64 ± 4.09	44.08 ± 2.36	0.000*
No act (n)	0	0	
Medial dorsal cutaneous			
Amplitude (μV)	3.92 ± 0.68	2.41 ± 0.75	0.000*
NCV (m/sn)	43.92 ± 1.49	39.56 ± 2.50	0.000*
No act (n)	0	0	
Dorsal sural			
Amplitude (μV)	6.61 ± 1.06	3.96 ± 1.18	0.000*
NCV (m/sn)	50.81 ± 3.12	41.48 ± 2.36	0.000*
No act (n)	0	0	

NCV nerve conduction velocity. * p<0.001(Mann Whitney U)

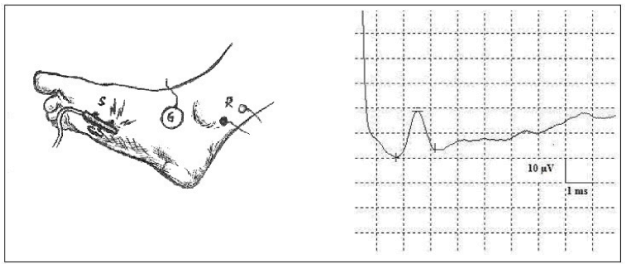

Figure 1. Medial plantar nerve conduction technique and a medial plantar nerve SNAP recording from a control subject (S, stimulating electrode; R, recording electrode; G, ground electrode)

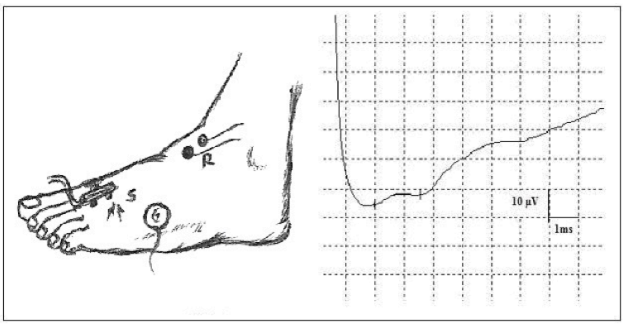

Figure 2. Medial dorsal cutaneous nerve conduction technique and a medial dorsal cutaneous nerve SNAP recording from a control subject (S, stimulating electrode; R, recording electrode; G, ground electrode)

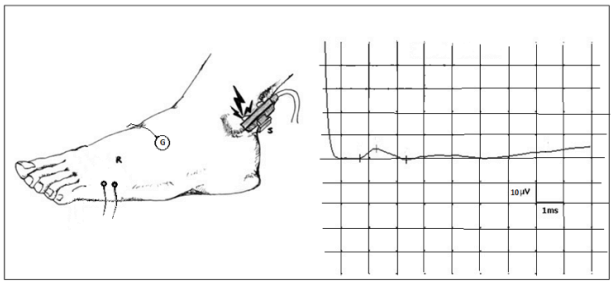

Figure 3. Dorsal sural nerve conduction technique and a dorsal sural nerve SNAP recording from a control subject (S, stimulating electrode; R, recording electrode; G, ground electrode)

also measured.

c) The DS nerve was stimulated using a felt electrode to study the former's sensory conduction and the antidromic recordings were made from the surface electrodes placed at the distal part of the fifth metatarsal bone on the dorsum of foot.

Statistical analysis

The statistical analyses of the study data were performed with SPSS (Statistical Package for Social Sciences) Windows 11.5 software package. A P value less than 0.05 was considered statistically significant. Descriptive statistics (mean, standard deviation), Mann Whitney U test, and Independent samples T-test was used for evaluation of the study data.

Results

Our study enrolled a total of 35 Type II Diabetes patients (20 females, 15 males) with a mean age of 47.22±8.15 years and 30 healthy controls (17 females and 13 males) with a mean age of 49.30±6.56 years. The two groups did not significantly differ with respect to age and sex ($p>0.05$). The routine study protocol including the motor NCS of bilateral posterior tibial, peroneal, median, and ulnar nerves and the sensory NCS of bilateral sural, median, and ulnar nerves were within the normal limits and similar in both groups ($p>0.05$).

MP, DS, and MDC nerve action potentials were obtained in all subjects. The results of the DS, MP, and MDC sensory NCS were compared between the patient and control groups. The control group had a DS nerve mean amplitude of 6.61 μV, a MP nerve mean amplitude of 8.23 μV, and a MDC nerve mean amplitude of 3.92 μV.

The diabetic group had a DS nerve mean amplitude of 3.96 μV, a MP nerve mean amplitude of 3.95 μV, and a MDC nerve mean amplitude of 2.41 μV. The diabetic group had a significant decrease in the amplitudes of each of the three nerves when compared to the control group ($p<0.001$).

The control group had a DS mean nerve conduction velocity (NCV) of 50.81 m/sn, a MDP mean NCV of 55.64 m/sn, and a MDC mean NCV of 43.92 m/sn.

The diabetic patient group had a DS mean NCV of 41.48 m/sn, a MP mean NCV of 44.08 m/sn, and a MDC mean NCV of 39.56 m/sn. The diabetic patients showed significant slowing in each of the three nerves compared to the control group ($p<0.001$).

Discussion

The signs of diabetic neuropathy may not be evident on routine electrophysiological studies performed early in the course of the disorder and electrophysiological diagnosis becomes difficult in patients who are either asymptomatic or newly and slightly symptomatic [4]. The PNP has been reported to have a prevalence of 7% in the first year after the diagnosis of DM and 50% in a 25-year follow-up. Adding EMG and other ancillary tests to clinical evaluation results in a prevalence in excess of 60%; the rate even reaches 90% when subclinical cases are also considered [5].

Our study demonstrated impaired DS, MDC, and MP nerve studies despite normal routine electrophysiological studies in newly diagnosed Type II DM. This finding is in agreement with the knowledge that DS, MDC, and MP nerves are the most distal sensory nerves and confirms the results of the previous studies suggesting that early pathologic events are more evident in the most distal part of the sensory fibers [6,7]. Hence, as stated above, detecting subclinical PNP in DM at an early stage is possible via conduction studies on the most distal nerves. Although there are a plenty of electrophysiological studies in the literature examining diabetic neuropathy, studies investigating the DS nerve conduction are limited. DS nerve conduction studies were first defined in 1974 by Burke et al. who reported that DS nerve values are highly variable [8].

Our study revealed a mean MP nerve conduction velocity of 50.81±3.12 m/sec and a lower limit of 44 m/sec. Of the 35 patients with diabetes, 14 patients had a MP NCV less than 44 m/sec. Our results thus demonstrated that 40% of the diabetes group could be neurophysiologically diagnosed with PNP despite normal conventional nerve conduction studies. Leventoğlu et al. also found a significantly slower DS nerve conduction velocity in an early-stage type II diabetes patients who had neuropathic complaints consistent with PNP compared to normal values in routine electrophysiological studies compared to the control group [9]. Similar to that, we also showed a slowing in DS NCV, although our patients were neurologically asymptomatic. This suggests that approximately 40% of patients with newly diagnosed type 2 DM who have no neuropathic complaints have electrophysiological abnormalities.

Killian and Foreman (2001) studied bilateral sural and DS nerve conduction antidromically in 70 patients with PNP of non-diabetic origin (alcoholic, autoimmune, arteritis, or drug-induced) having sensory symptoms and one or more clinical signs and in 38 controls. They found that the sural sensory action potentials could not be detected or were found reduced in 77% of the patients, while 23% of the patients had normal sural sensory action potentials. Bilateral dorsal sural amplitudes were not detectable in 97% of seventy patients. They demonstrated that DS nerve may have been affected before pathology emerges in sural nerve [10]. Kökoğlu et al. detected a slowing in DS NCV in the patient group compared to the control group in early-stage diabetic neuropathy [11].

Uluç et al. found significantly lower amplitudes and conduction velocities of DS and MP sensory nerve responses in patients with diabetic sensory neuropathy and normal routine electrophysiological studies [12]. Our results were in agreement with that study, although our patients had no symptoms suggestive sensory neuropathy.

Our study revealed a mean MP NCV of 55.64±4.09 and a lower limit of 44 m/sn. Of the 35 patients with diabetes, 14 patients had a MP NCV less than 44 m/sec. Thus, according to our study, 40% of the diabetes group could be neurophysiologically diagnosed with PNP despite normal conventional nerve conduction studies.

In our study, the control group had a mean MDC NCV of 43.92±1.49 and a lower limit of 40 m/sn. Of the 35 patients with diabetes, 14 patients had a DS NCV less than 40 m/sn. Thus, according to our study, 40% of the diabetes group could be neurophysiologically diagnosed with PNP despite normal conventional nerve conduction studies.

In another study Altun et al. compared DS and MDC nerve conduction in patients diagnosed with diabetic PNP and reported that DS nerve conduction was more sensitive [13].

We neurophysiologically detected asymptomatic PNP in diabetic patients by studying nerve conduction properties of the three most distally located nerves (MP, DS, MDC) in addition to the classical nerve conduction studies in patients with newly diagnosed diabetes and without neurological symptoms. While the results of the classical nerve conduction studies were normal in early stage diabetes, the earliest signs of polyneuropathy existed in the form of a slowing in the sensory conduction velocities and a slight reduction in the amplitudes of the sensory action potentials in the MP, MDC, and DS nerves.

Among these three nerve conductions, MP and DS sensory nerve conduction velocities were significantly lower than that of MDC. Furthermore, that measurement of the MDC nerve conduction is technically more demanding and its conduction cannot be detected physiologically even in normal persons at an advanced age suggests that the other two nerve conductions are more sensitive and reliable. However, we could obtain MP, DS, and MDC nerve conduction responses in both the

control group and the diabetic patients, which suggests the importance of these nerves in putting the diagnosis of early stage PNP.
In conclusion, it may be possible to detect the pathology in a neurophysiological manner in asymptomatic diabetic PNPs at an early stage by studying MP and DS sensory nerve conduction properties in addition to the nerve conduction parameters studied in a standard PNP protocol at ENMG laboratory. Revealing PNP at an asymptomatic period by means of these methods may aid in taking measures before progression into symptomatic PNP.

Scientific Responsibility Statement
The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest
None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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